REMARKS

I. Status of the Claims

Claims 1-17 are pending. Claims 14-17 have been withdrawn by the Office for purportedly being drawn to non-elected invention. Claims 2 and 3 are amended to correct minor formality inconsistencies. Claims 1-13 are under examination on their merits.

II. Priority

Applicant acknowledges the Office's determination that the effective filing date of the pending claims to be February 20, 2004, the filing date of the earliest provisional application Serial No. 60/546,227.

III. Claim Rejections under 35 U.S.C. §102

The Action rejects claims 1-13 under 35 U.S.C. §102(e) as being anticipated by Barone et al. (WO 2004/105751, hereinafter "Barone"). Specifically, the Action asserts that Barone teaches a method of treating hypertension in a mammal, comprising administering to the mammal an effective amount of a PDE4 inhibitor such as rolipram. The Action further asserts that the method of Barone implicitly encompasses patients suffering from all types of hypertension including salt-sensitive hypertension. Moreover, the Action asserts that Weinberger et al. (Hypertension, 1986, 8 (Suppl II): II-127-II-134) teaches that more than 51% of patients with hypertension are classified as salt-sensitive. Thus, the Action concludes, Barone teaches treatment of hypertension with rolipram.

Applicant respectfully traverses the rejection. As a threshold matter, the Federal Circuit has stated that for prior art to anticipate under section 102, every element of the claimed invention must be identically disclosed in a *single* reference. *Corning Glass Works v. Sumitomo Electric*, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989) (emphasis added). The exclusion of a claimed element, no matter how insubstantial or obvious, from a reference is enough to negate anticipation. *Connell v. Sears, Roebuck & Co.*, 220 U.S.P.Q 193, 198 (Fed. Cir. 1983). For at least the following reasons, Applicant respectfully contends that Barone is not an anticipatory art.

A. Barone does not explicitly or implicitly teach every element of the claimed invention

The disclosure in the Barone reference is much more limited than the Action asserts. For one thing, the reference merely discloses a method of treating cardiac hypertrophy with a

PDE inhibitor. The Action credits speculation made in Barone that a PDE inhibitor might be used to treat other cardiovascular pathologies in a mammal; however, the Office misinterprets the teachings of the reference, which do not anticipate the claimed invention of using a PDE inhibitor to treat *hypertension*.

The Barone reference sets forth a long list of "cardiovascular pathology" for which PDE inhibitors are purportedly suitable for treating. *See* page 3, lines 16-19. The list includes "cardiac hypertrophy, coronary heart disease, arrhythmia, restricted coronary blood flow, arteriosclerosis, heart failure, congestive heart failure (CHF), myocardial infarction, as well as others." Thus, on its face the Barone reference contains no express teachings that *hypertension* belongs on the list of cardiovascular ailments that can be treated by a PDE inhibitor. Indeed, not only does the reference not teach this method, but it affirmatively omits hypertension from the enumerated list of cardiovascular pathologies for which PDE inhibitor treatment is asserted to be effective. The Office has read into the reference teachings that simply are not there.

The Office nevertheless points to claims 1, 5 and 7-8 for the asserted anticipatory teaching. The corresponding disclosure of the referenced claims can be found on page 10, lines 14-18 of the Barrone reference, which is reproduced below:

> *Thus, one aspect of the present invention is a method of reducing cardiovascular pathology in a mammal, comprising administering an amount effective for reducing said cardiovascular pathology with a phosphodiesterase 4 (PDE4) inhibitor. In another aspect of the invention, the cardiovascular pathology is cardiac hypertrophy, heart failure, and/or CHF. In another aspect, the mammal <u>is suffering from hypertension</u> and/or arteriosclerosis.*

(Emphasis added.) Applicant respectfully contends that the mere mention of a method for reducing cardiovascular pathology in a mammal, wherein, in one aspect the cardiovascular pathology is cardiac hypertrophy, and in another aspect the mammal "is suffering from hypertension," does not explicitly teach a method of reducing hypertension using a PDE inhibitor. Indeed, nowhere in Barone does the reference explicitly teach a method of treating hypertension using a PDE inhibitor.

Further, Barone does not even implicitly teach the claimed method because, *inter alia*, the reference does not enable one of ordinary skill in the art to carry out the claimed method of treating hypertension using a PDE inhibitor.

B. Barone does not enable one of ordinary skill in the art to carry out the claimed invention

A patent claim "cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1325 (Fed. Cir. 2005). The prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation. *Id.* *See also Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Education & Research*, 68 U.S.P.Q. 2d 1373, 1376 (Fed. Cir. 2003). With regard to undue experimentation, the court in *Elan Pharmaceuticals* referred to the factors delineated in *In re Wands* in determining enablement of a prior art. *Id.* (citing *In re Wands*, 858 F.2d 731, 737).

Simply put, it is insufficient for a purportedly anticipating reference to simply name or describe the desired subject matter, if it cannot be produced without undue experimentation. *Elan Pharmaceuticals*, 68 U.S.P.Q. 2d at 1376. (These principles are even more compelling where, as here, the cited Barone reference failed even to name or describe the claimed method of treating hypertension using a PDE inhibitor.) The principles underlying application of the criteria of enablement to the content of the prior art were discussed in *In re Donahue*, in which the Federal Circuit stated:

> It is well settled that prior art under 35 U.S.C. 102(b) must sufficiently describe the claimed invention to have placed the public in possession of it. Such possession is effected if one of ordinary skill in the art *could have combined the publication's description of the invention with his own knowledge* to make the claimed invention. Accordingly, even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it is not enabling.

In re Donahue, 766 F.2d 531, 533 (Fed. Cir. 1985) (emphasis added). The determination of what level of experimentation is "undue," so as to render a disclosure non-enabling, is made from the viewpoint of a person experienced in the field of the invention. *Elan Pharmaceuticals*, 68 U.S.P.Q. at 1376. Applicant respectfully submits that, in view of the attached Declaration by Dr. Danziger, one of skilled in the art could not have combined Barone's description with her own knowledge to carry out the claimed invention. Therefore, one of skilled in the art would not have considered Barone an enabling art that has placed the public in possession of the claimed invention.

Inventor Dr. Danziger in his Declaration explains that, due to the multi-faceted etiologies of hypertrophy known to workers of ordinary skill in the art, a drug that is purportedly effective in treating hypertrophy does not necessarily reduce hypertension. Dr.

Danziger further avers that even if the hypertrophy is caused by hypertension, a drug that alleviates hypertrophy does not necessarily alleviate the underlying *cause* of hypertrophy, *i.e.*, hypertension. For example, both the endothelin receptor antagonist BQ123 and the antioxidant N-2-mercaptopropionyl glycine (MPG) have been shown to reduce hypertension-induced cardiac hypertrophy but ineffective in alleviating the underlying hypertension. *See* paragraph 9 of the Declaration.

Similarly, as Dr. Danziger points out in his Declaration, in a mammal that experiences hypertrophy and is suffering from hypertension, a drug that is effective in treating hypertrophy does not necessarily reduce hypertension. *See* paragraphs 10 and 11 of the Declaration. For example, angiotensin II induces hypertrophy as well as hypertension in a mouse model. *See* paragraph 11 of the Declaration. The antioxidant, N-acetylcysteine (NAC), was shown to reduce angiotensin II-induced hypertrophy in mice; however, NAC was ineffective in reducing angiotensin II-induced hypertension in the same mouse model. *Id.*

Thus, it has long been known that drugs, such as BQ123, MPG, and NAC that are effective in treating hypertrophy do not necessarily reduce hypertension. The Barone reference itself does not demonstrate that a PDE inhibitor can reduce hypertension, let alone salt-sensitive hypertension. Thus, one of ordinary skill in the art would not have combined Barone's insufficient description with her own knowledge to carry out the claimed invention. Accordingly, Barone does not provide sufficient description to have put the claimed invention in possession of the public, and thus does not anticipate the claimed invention.

Accordingly, Applicant respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e) based on Barone.

CONCLUSION

Applicant believes that the condition for allowance has been met. A most favorable decision is earnestly solicited.

If the Examiner deems it helpful, the Examiner is invited to contact undersigned representative at 312-913-0001.

Respectfully submitted,

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